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EXAMINER	
MARSCHEL, A	
ART UNIT	**PAPER NUMBER**
1807	15

DATE MAILED: 10/21/91

MORGAN & FINNEGAN
345 PARK AVENUE
NEW YORK, NY 10154

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 6/24/91 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), _____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 104-109, 113-118, 125-137, and 140-144 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 104-109, 113-118, 125-137, and 140-144 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 1800, Art Unit 1807.

Applicant's arguments filed 6/24/91 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either newly applied or reiterated. They constitute the complete set presently being applied to the instant application.

The instant application contains numerous minor errors that are either typographical errors, misspellings, or scientific omissions/errors. Although these appear to be minor, they introduce unclarities that may weaken the clear and concise description of the invention disclosed therein. The Examiner requests that applicant(s) review the disclosure and amend these minor aspects to remove the errors without adding new matter. Some examples of these minor errors are as follows:

On page 1, line 8, the element "phosphorous" appears to be misspelled.

On page 5, line 30, one of the options for "x" is "H-". This option for "x" is not clarified elsewhere and appears to be an incorrect option for "x" in the context of the instant disclosure wherein there is no operational discussion of 5'-deoxynucleotides. This is included herein to clarify its presence in the specification but this is not a minor error since it is the basis of one of the rejections given below.

On page 12, lines 8-9, the word "interracting" appears to be misspelled.

On page 12, line 11, the word "moeities" appears to be misspelled.

On page 30, line 24, the word "Haptene" appears to be misspelled.

On page 33, line 29, the word "reitterated" appears to be misspelled.

On page 33, line 30, the species name "milanogaster" appears to be misspelled.

On page 43, lines 18-19, the word "Occaionally" appears to be misspelled.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claim 140 was not amended in the claims section of the amendment filed 6/24/91. Therefore the replacement page for claim 140 that does not contain a "taped on" structure was not entered. Thus, claim 140 with the "taped on" structure remains as claim 140. Correction is requested.

Although not clearly claimed, the Examiner deems that applicants possibly intend that "H-" be one of the options for "x" as given in claim 140, line 25. There is a lack of any enablement of such a 5' terminus in the instant disclosure.

Claims 140 and 141 cite structures where the "z" moiety is mono-, di-, or tri-phosphate. Such structures completely lack enablement in the instant specification.

Claims 140 and 141 are rejected under 35 U.S.C. § 112, first

paragraph, for the reasons set forth in the objection to the specification.

Claims 104-109, 113-118, 125-137, and 140-144 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to "A" moieties consisting essentially of either iminobiotin or biotin. All of the claims are rejected, including claim 105, because of the open claim language term "comprises" cited in line 2 of claim 125 as well as line 2 of claim 105. The clear and concise enablement of "A" beyond said iminobiotin and biotin is lacking due to the citation of several of the structures given in the specification on page 12. For example, on page 12, at line 27, the lefthand structure is shown as having two unattached bonds, one at each end of the structure, whereas all the other "A" examples have only one bond available for attachment to the linker or nucleoside base. The said two bond example of "A" prevents a clear and concise enablement of the moiety "A" since there is no discussion of a two bond attachment to "A" from either the linker or nucleoside base. Additionally, on page 13, lines 1-3, a problem with aromatic "A" moieties is cited as intercalation. This is never resolved as to how the aromatic structures on page 12, line 20, for example, are enabled versus other aromatic structures. What criteria of intercalation should be used to resolve this issue? No such test is discussed in the instant specification. As added support for the undue experimentation with regard to the practice of "A" moieties, the Examiner wishes to note the several

"essential criteria" listed on page 9, line 1, through page 10, line 19. Satisfaction of all of these criteria is clearly undue experimentation, especially since the practice of satisfying these criteria is not clearly and concisely enabled in the instant specification. See the below rejection under 35 U.S.C. § 112, second paragraph, for a number of unclarities as to what is meant in practicing the selection of "A" moieties. See M.P.E.P. §§ 706.03(n) and 706.03(z).

Applicants argue the above rejection in the amendment filed 6/24/91 by noting the page 12 structures. This argument has been answered by noting the specific enablement difficulties of these structures beyond biotin or iminobiotin as discussed above. This also brings into question the enablement of the disulfide containing structure of page 12, at line 27, righthand column, since the practice of satisfying the "essential criteria" is not clearly and concisely discussed for this structure either. Applicants cite U.S. Patent No. 4,067,774 and British Patent No. 1 564 578 in support of enablement. These citations are moot to overcome the above enablement rejection since the disclosures are cleanly directed to the listing of well known antigens. The rejection is based on the undue experimentation needed to satisfy the several "essential criteria" given in the specification on pages 9-10 and not whether there are many known antigens.

Applicants go on to argue that claims need not be limited to "A" moieties that are specifically exemplified. The Examiner wishes to note that in order to obtain a claim scope beyond the

exemplified "A" moieties, clear and concise enablement of such a broad scope is needed. As discussed above, the clear and concise enablement beyond the exemplified "A" moieties is lacking in the instant specification. Therefore the rejection is maintained as proper.

Claims 104-109, 113-118, 125-137, and 140-144 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The structure in claim 125 is vague and indefinite because the third ribose moiety lacks the "z" group at the 2' position as given on the other ribose moieties as well as in the previous claim 125 prior to the amendment filed 6/24/91. Correction of this conflict is requested.

Claim 140 cites the moiety "H-HO-" as one of the represented options for "x, y and z". This structure is vague and indefinite as to what is meant.

What are the metes and bounds of the "A" moiety instantly claimed? On page 9, line 1, through page 10, line 19, the specification describes several criteria for the modified nucleotide residues. On page 9, lines 11-12, the analogs are described as having to be "relatively efficient substrates for commonly studied nucleic acid enzymes". What are the metes and bounds of the phrase "relatively efficient"? Is simple detection of usability as substrates sufficient? If so, this is not discussed in the specification. What criteria is used to meet

the "relatively efficient" practice? None is given in the instant specification. On page 10, lines 4-10, the phrase "...probe substituents should not be significantly altered so that currect procedures using radioactive hybridization probes need not be extensively modified". What are the metes and bounds of the phrase "not extensively modified"? The Examiner finds this statement in conflict with the practice of the instant invention in that the conversion to a non-radioactive assay from a radioactive assay is clearly an extensive modification of the assay methodology. Lastly, how is it possible to design a linkage that will withstand "all experimental conditions to which normal nucleotides and polynucleotides are routinely subjected..."? Aren't polynucleotides frequently and routinely subjected to strong acid, for example during precipitations, as a common laboratory procedure? Do applicants mean to limit the experimental procedures to certain hybridization assay types? If so, this is not stated in the specification. Clarification of the claim language is requested as to what is meant to be claimed in the instant invention.

In claim 126, line 3, the target is cited as being a "nucleic acid sequence". This is vague and indefinite since a "nucleic acid sequence" is a mathematical representation of a polynucleotide and not a composition. How can the target be a mathematical representation? This vague and indefinite citation is present in several other claims also. Clarification of the claim language is requested.

Claim 140 is vague and indefinite in that a "cyclic moiety" is cited in line 28, followed by a depiction of a structure which is not cyclic. Clarification of this conflict is requested.

In reviewing the instant application, it is noted by the Examiner that an Information Disclosure Statement was filed in the instant application on 8/7/89 but that the PTO Form 1449 filed in said Statement has not been executed. It is also noted that applicants stated that copies of the references listed on said PTO Form 1449 had previously been supplied in connection with the prosecution of the parent application serial number 06/496,915. The file for serial number 06/496,915 has been requested by the Examiner but has not yet been received by the Examiner as of the mailing of this office action.

Applicants have cited two references in their amendment filed 6/24/91. These references have been cited on the enclosed PTO Form 892 to make them of record in the instant application. As a courtesy to the Examiner, it is requested that in the future such submitted references be listed on a PTO Form 1449 to make them of record.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

The CM1 Fax Center number is (703) 308-4227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

October 18, 1991

Ardin Marschel

ARDIN MARSCHEL
PATENT EXAMINER
ART UNIT 1807